UNC CANCER NETWORK

CANCER TREATMENT IN NORTH CAROLINA **RESEARCH TO PRACTICE**

Live Lecture

April 22, 2020

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2

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UNC CANCER NETWORK

CANCER TREATMENT IN NORTH CAROLINA **RESEARCH TO PRACTICE**

April 22, 2020

Head and Neck Cancer Management in North Carolina: Updates for 2020

Siddharth Sheth, DO, MPH

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OUR PRESENTER

Siddharth Sheth,
DO, MPH

Dr. Sheth is a medical oncologist and clinical and translational researcher. He is a member of the Head and Neck and Phase I Disease Groups at the University of North Carolina at Chapel Hill.

His research focuses on the evaluation of novel therapies for patients with head and neck cancers in clinical trials, particularly focusing on novel immunotherapy and targeted therapies.

He also participates in trials to improve treatment options for patients with rarer head and neck tumors including salivary and thyroid malignancies.

His translational science focuses on the studying circulating tumor DNA (ctDNA) to evaluate response to therapy and monitoring for disease recurrence.

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Respond at **PollEv.com/unccn**

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UNC CANCER NETWORK

- **Which one of the following is NOT a cancer of the head and neck region?**

Oral cavity	**A**
Pharynx	**B**
Spleen	**C**
Salivary glands	**D**

Answers to this poll are anonymous

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DISCLOSURES

This activity has been planned and implemented under the sole supervision of the course directors, in association with the UNC Office of Continuing Professional Development (UNC CPD). William A Wood, MD, MPH, and CPD staff have no relevant financial relationships with commercial interests as defined by the ACCME.

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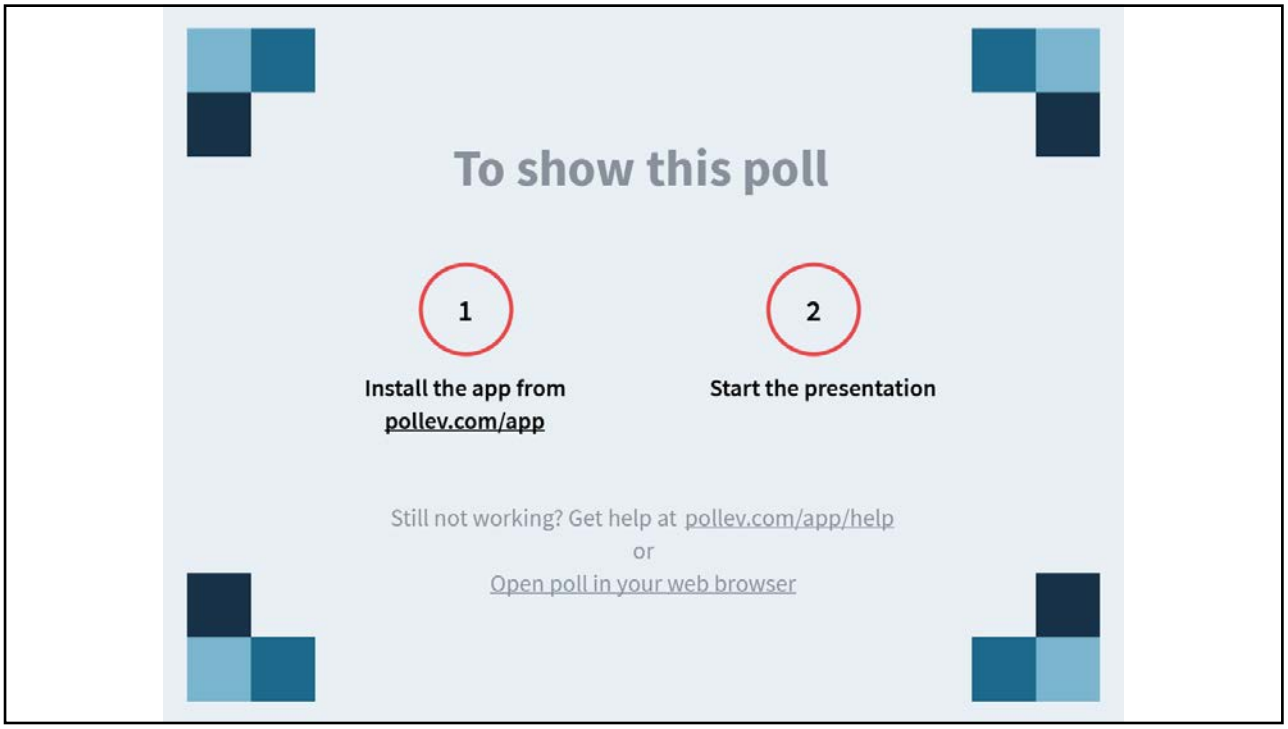

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Head and Neck Cancer Management in North Carolina: Updates for 2020

Siddharth Sheth, DO MPH
Assistant Professor of Medicine & Otolaryngology
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UNC LINEBERGER COMPREHENSIVE CANCER CENTER
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Disclosures

None.

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Historically

2020

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Case

Ramses T. Heel is a 55 year old white male who presents for follow up. You initially met him three weeks ago after he discovered a painless neck mass while shaving. He has noted "on and off" sore throat for the last 2 months but thought it was allergies. He denies any other symptoms including pain with swallowing, shortness of breath or weight loss.

His past medical history (PMH) is significant for asthma and well controlled hypertension on lisinopril. He has a 5 pack year smoking history during college (1980s) and drinks alcohol socially. His family history is significant for breast cancer (mother and older sister). He travels to China yearly for business for the last 10 years.

You ordered a CT neck, which showed a 3cm mass and subsequently referred him to ENT. Endoscopic evaluation reveals a 1 cm right tonsillar mass. An ultrasound guided FNA was performed in office. Pathology returned positive for squamous cell carcinoma. Additional diagnostic testing is pending.

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Question #1

55 y/o WM p/w painless neck mass. PMH HTN & asthma; FamHx breast ca. SocHx +5 PYH, social EtOH use, +China travel. CT with 5cm neck mass. FNA +SCC

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Question #1

Which of the following is not a risk factor for head and neck cancer?

1. Smoking
2. Alcohol use
3. Age
4. Yearly travel to China
5. Human papilloma virus (HPV)

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Learning Objectives

- Understand key risk factors and critical anatomy associated with head and neck cancers
- Distinguish differences in biology, prognosis, and treatment between HPV associated head and neck cancer and non-HPV associated head and neck cancer
- Recognize and familiarize findings from seminal head and neck cancer clinical trials in the last 2 years

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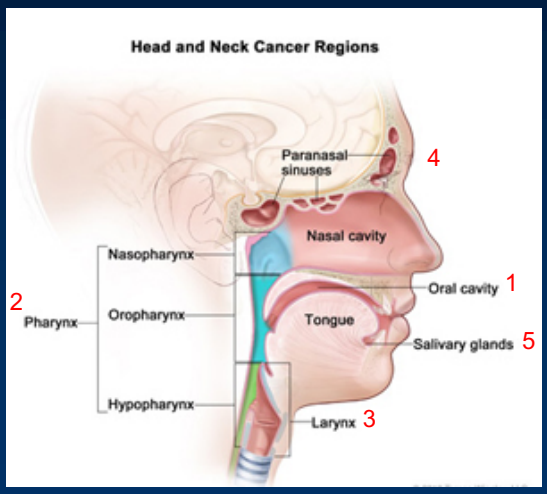
Head and Neck Cancer Anatomy

- Pathology: SCC
- 5 main anatomical locations
- Location is influenced by risk factor



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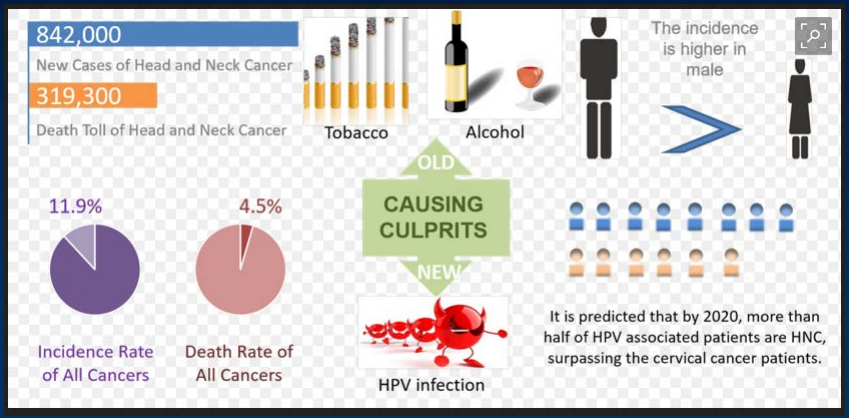
Statistics and Epidemiology



ACS Facts and Figures, 2018; Advanced Science News, 2017

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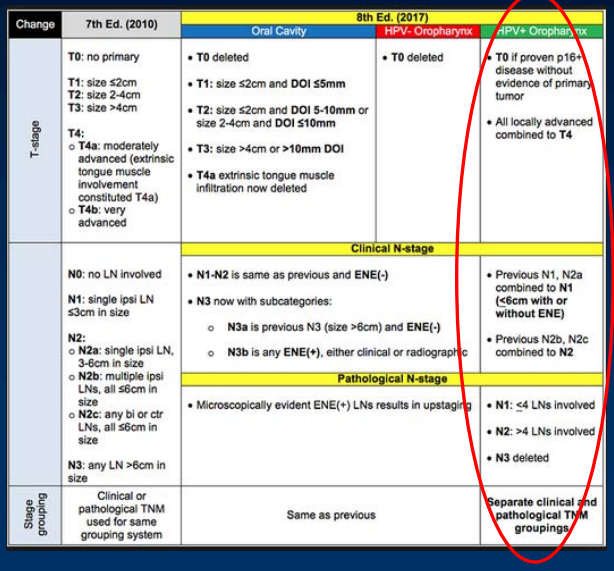
HNSCC TNM Staging is Complex



Change	7th Ed. (2010)	8th Ed. (2017) Oral Cavity	8th Ed. (2017) HPV- Oropharynx	8th Ed. (2017) HPV+ Oropharynx
T-stage	**T0**: no primary **T1**: size ≤2cm **T2**: size 2-4cm **T3**: size >4cm **T4**: ○ **T4a**: moderately advanced (extrinsic tongue muscle involvement constituted T4a) ○ **T4b**: very advanced	• **T0** deleted • **T1**: size ≤2cm and **DOI ≤5mm** • **T2**: size ≤2cm and **DOI 5-10mm** or size 2-4cm and **DOI ≤10mm** • **T3**: size >4cm or **>10mm DOI** • **T4a** extrinsic tongue muscle infiltration now deleted	• **T0** deleted	• **T0** if proven p16+ disease without evidence of primary tumor • All locally advanced combined to **T4**
		Clinical N-stage		
	N0: no LN involved **N1**: single ipsi LN ≤3cm in size **N2**: ○ **N2a**: single ipsi LN, 3-6cm in size ○ **N2b**: multiple ipsi LNs, all ≤6cm in size ○ **N2c**: any bi or ctr LNs, all ≤6cm in size **N3**: any LN >6cm in size	• **N1**-**N2** is same as previous and **ENE(-)** • **N3** now with subcategories: ○ **N3a** is previous N3 (size >6cm) and **ENE(-)** ○ **N3b** is any **ENE(+)**, either clinical or radiographic		• Previous N1, N2a combined to **N1 (≤6cm with or without ENE)** • Previous N2b, N2c combined to **N2**
		Pathological N-stage		
		• Microscopically evident ENE(+) LNs results in upstaging		• **N1**: ≤4 LNs involved • **N2**: >4 LNs involved • **N3** deleted
Stage grouping	Clinical or pathological TNM used for same grouping system	Same as previous		**Separate clinical and pathological TNM groupings**

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Rate of metastatic disease at initial presentation for common cancers

Site	Metastatic Rate (%)	Source
Breast Cancer	6-10%	MBCN.org 2016
Colorectal Cancer	25%	Engstrand. BMC Cancer. 2018
Cervical Cancer	13%	Li. J Gynecol Oncol. 2016
NSCLC	25-40%	ACS 2017
Pancreatic Cancer	30-50%	ACS 2018
Prostate Cancer	5%	ACS 2018

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HNSCC rarely presents as metastatic disease

Site	Total in SEER	Number Metastatic at Presentation	Percentage	95% CI
Lip	5,975	20	0.33%	0.20-0.52%
Oral Cavity	16,385	320	1.95%	1.75-2.18%
Oropharynx	17,783	729	4.10%	3.81-4.40%
Hypopharynx	1,866	128	6.86%	5.75-8.10%
Supraglottis	8,114	270	3.33%	2.95-3.74%
Glottis	13,085	87	0.66%	0.53-0.82%
Subglottis	356	12	3.37%	1.75-5.81%
Sinus	1,068	69	6.46%	5.06-8.11%
Nasopharynx	2,610	177	6.78%	5.85-7.81%

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Non-metastatic HNSCC

- Stage at diagnosis: early stage (40%) and locally advanced (LA), 50%)
- Prognosis for LA-HNSCC remains poor
- Treatment options:
  1. Primary surgery followed by post-operative RT ± chemotherapy
  2. Concurrent chemoradiation therapy (cCRT)

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HPV-ASSOCIATED HNSCC

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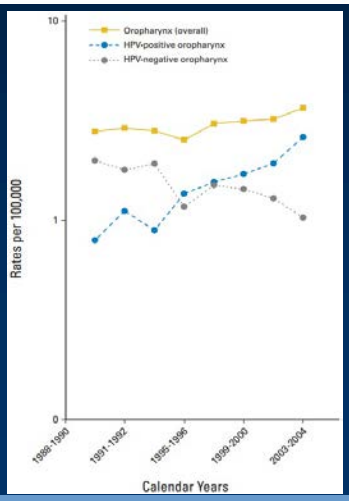
HPV and the rise of oropharynx cancer in the US

VOLUME 29 · NUMBER 32 · NOVEMBER 10 2011
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT



↑28% in <u>all</u> OPSCC
2.6→3.6 cases/100k

↑225% in HPV+ OPSCC
0.8→2.6 cases/100k

↓50% in HPV- OPSSC
2.0→1.0 cases/100k

Chatruvedi et al, J Clin Oncol, 29(32), 2011

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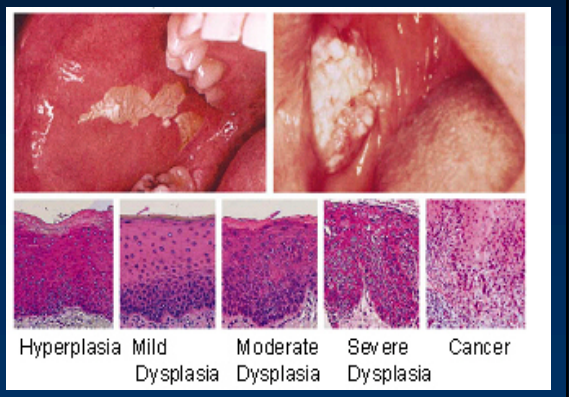
What is HPV?

- >100 types of HPV have been classified to date
  - HPV 16 is most commonly associated with OPSCC
  - Sometimes HPV 18, 31 or 33
  - Rarely other “high risk” types
- Also causes gynecological, anal, penile cancers
- HPV DNA is detected in 65% of OPSCC (tonsil & base of tongue)



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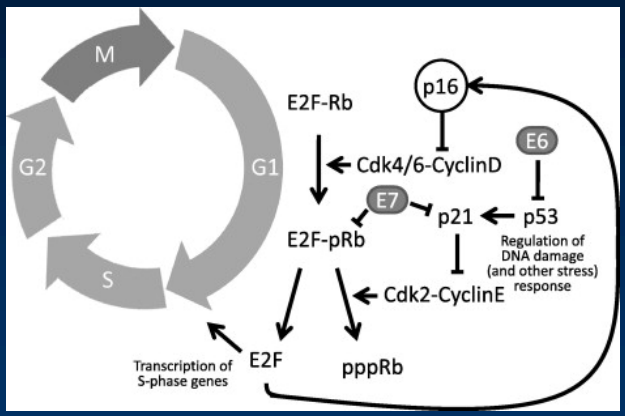
Viral oncogenes and p16 expression

- E6/E7 viral oncoproteins
  - E6 inactivates p53
  - E7 inactivates Rb
- Over expression of E2F leading to p16 expression
- >80% malignant cells positive by p16 IHC correlates with HPV+



Chan PK et al, *Crit Rev Clin Lab Sci* 49:117, 2012;
Darragh TM *et al*, *Arch Pathol Lab Med* 136:1266, 2012

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How to test for HPV?

Base of Tongue/Tonsil/Posterior Pharyngeal Wall/Soft Palate WORKUP

- Tumor human papillomavirus (HPV) testing by p16 immunohistochemistry (IHC) required[a]
- H&P[b,c] including a complete head and neck exam; mirror and fiberoptic examination as clinically indicated
- Biopsy of primary site or fine-needle aspiration (FNA) of the neck
- CT with contrast and/or MRI with contrast of primary and neck
- As clinically indicated:
  - Preanesthesia studies
  - FDG-PET/CT
  - Chest CT[d] (with or without contrast)
  - Dental evaluation,[e] including Panorex
  - Nutrition, speech and swallowing evaluation/therapy, and audiogram[f]
  - EUA with endoscopy[g]

Multidisciplinary consultation as clinically indicated

p16-negative

p16 (HPV)-positive

[redacted]

Tests for HPV status
- p16 IHC
- HPV ISH
- HPV PCR

[redacted]

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2019
Cancer of the Oropharynx

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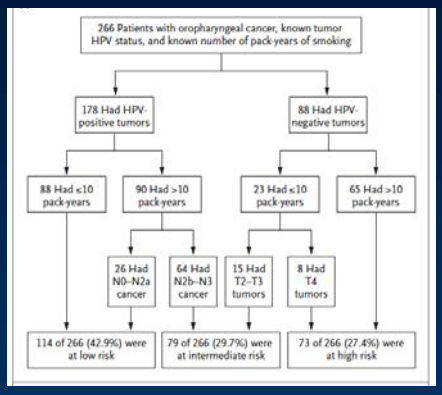
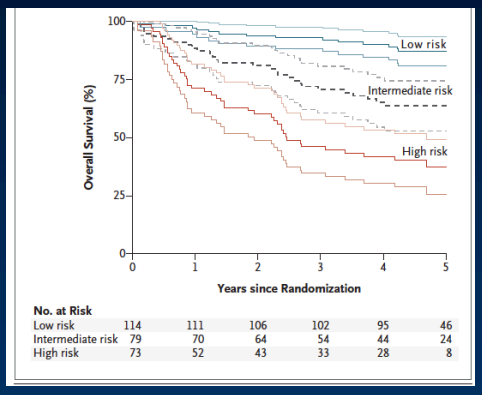
RTOG 0129: Risk Stratification in Oropharynx Cancer





	Low Risk	Intermediate Risk	High Risk
3 year OS	93%	71%	46%

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HPV and HNSCC prognosis

- 87% are HPV positive HNSCC are non-smokers and light drinkers
- Higher sensitivity to chemoradiation
- Independent predictor for overall survival
- Superior survival regardless of stage at diagnosis

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Treatment of HPV-associated HNSCC

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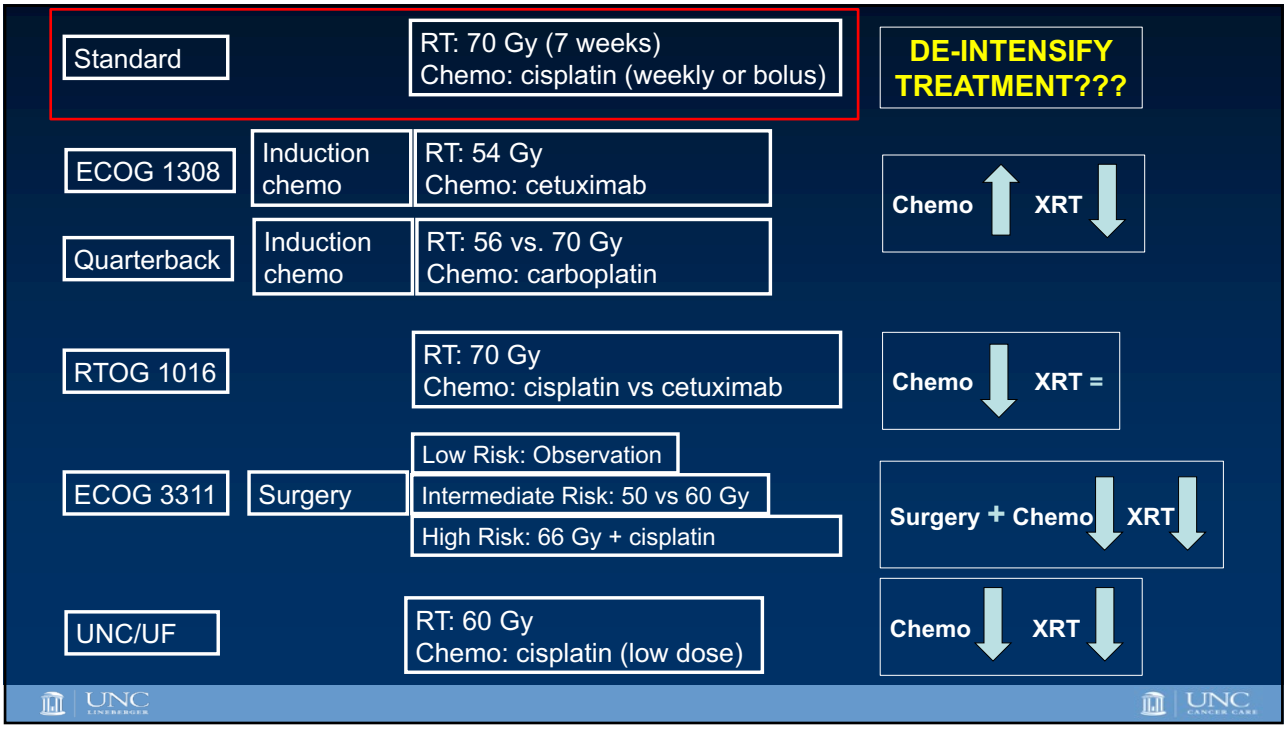

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Are All HPV-Associated OPSCC the same?

Phase II study of N=80 patients
- **Stage III/IV HPV-associated OPSCC**
- **Regardless of smoking status**

E1308: Phase II Trial of Induction Chemotherapy Followed by Reduced-Dose Radiation and Weekly Cetuximab in Patients With HPV-Associated Resectable Squamous Cell Carcinoma of the Oropharynx— ECOG-ACRIN Cancer Research Group

Neoadjuvant chemotherapy (3 cycles, every 21 days)
- Cisplatin 75mg/m2
- Paclitaxel 90 mg/m2
- Cetuximab 400 mg/m2 (cycle 1 day 1), then 250mg/m2 weekly

↓

Response to induction chemotherapy
- Primary site = manual and endoscopic
- Nodal sites = palpation

→ *70% had cCR at primary site (56 patients)*

↓

51 pts with cCR received cetuximab + 54 Gy
8 pts with <cCR received cetuximab + 54 Gy
9 pts w/o IC response received cetuximab + 70 Gy (SOC)

→ OUTCOMES?

UNC *J Clin Oncol 34. © 2016* UNC

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Table 3. Two-Year PFS and OS in Subsets Treated in the E1308 Trial

Cohort	2-Year PFS (95% CI)	2-Year OS (95% CI)
All patients (N = 80)	0.78 (0.67 to 0.86)	0.91(0.82 to 0.96)
cCR to IC, RRD 54 Gy (n = 51)	0.80 (0.65 to 0.89)	0.94 (0.84 to 0.99)
All cCR/PR/SD to IC, RRD ≤ 54 Gy (n = 62)	0.81 (0.69 to 0.89)	0.93 (0.83 to 0.97)
SRD[15]	0.67 (0.38 to 0.85)	0.87 (0.56 to 0.96)
Subsets cCR to IC, treated on RRD (n = 51)		
Cohort	0.90 (0.71 to 0.97)	0.97 (0.79 to 0.995)
Smoker > 10 pk-yr[21]	0.65 (0.41 to 0.82)	0.90 (0.66 to 0.97)
Smoker ≤ 10 pk-yr, and < T4N2c[21]	0.95 (0.71 to 0.99)	0.95 (0.71 to 0.99)
Smoker > 10 pk-yr or T4 or N2c[30]	0.69 (0.49 to 0.83)	0.93 (0.75 to 0.98)
Non-T4a (n = 45)	0.84 (0.69 to 0.92)	0.95 (0.83 to 0.99)
T4a[6]	0.50 (0.11 to 0.80)	0.83 (0.27 to 0.97)
N2c[15]	0.73 (0.44 to 0.89)	0.93 (0.61 to 0.99)
Non-N2c (n = 36)	0.82 (0.65 to 0.92)	0.94 (0.79 to 0.99)

Abbreviations: cCR, complete clinical response; IC, induction chemotherapy; pk-yr, pack-year; OS, overall survival; PFS, progression-free survival; PR, partial response; RRD, reduced radiation dose; SD, stable disease; SRD, standard radiation dose.

Median f/u = 35 months

Key Study Findings:

1. Outcomes were good with IC strategy and de-intensification of CRT
2. All HPV+ patients with recurrences occurred in those with >10 pack years smoking history

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Key Takeaways:

1. Risk factors matter for prognosis
2. Patients with HPV associated OPSCC who smoke <10 pack years are lowest risk.

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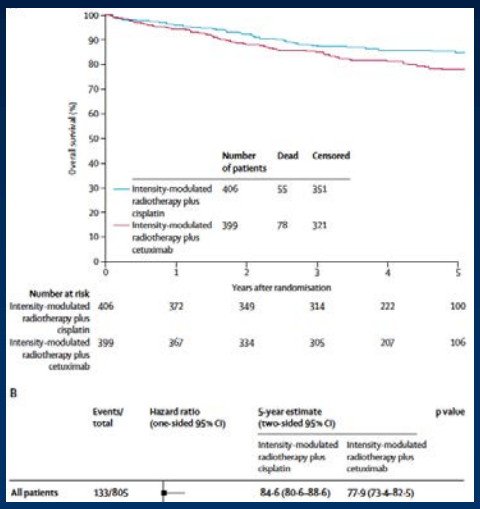
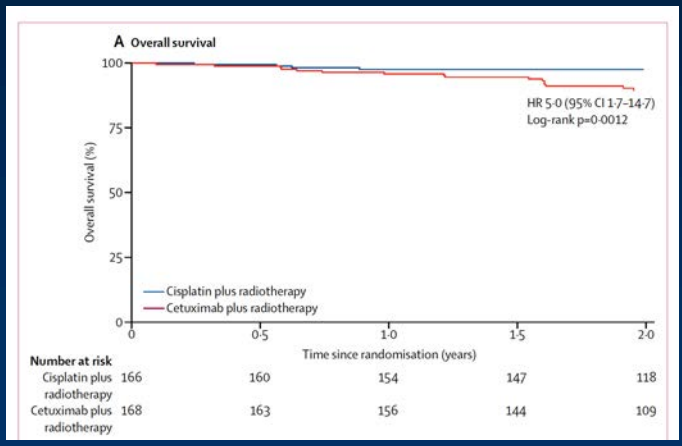
Does the type of systemic therapy matter?

70 Gy + Cetuximab vs. Cisplatin, HPV-associated OPSCC

RTOG 1016



De-ESCALaTE:



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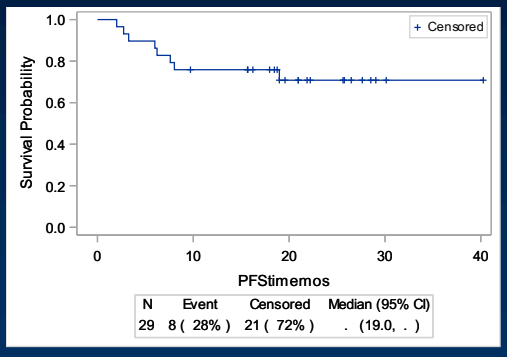
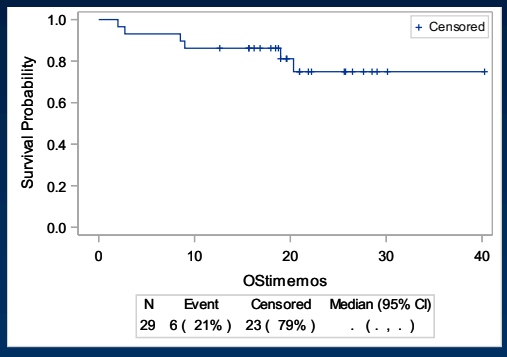
What about Radiation + Immunotherapy?

1 Year PFS = 76%



1 Year OS = 86%



Weiss J, Sheth S, et al. Concurrent definitive immunoradiotherapy for patients with Stage III-IV Head and Neck Cancer with cisplatin contraindication. Clinical Cancer Research. 2020. In Press.

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Key Takeaway:
In patients with HPV+ LA-OPSCC receiving curative therapy, cisplatin + radiation therapy remains the standard of care

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What about treatment options involving surgery?

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Phase II Evaluation of Aggressive Dose De-Escalation for Adjuvant Chemoradiotherapy in Human Papillomavirus–Associated Oropharynx Squamous Cell Carcinoma

Surgery followed by reduced RT dose

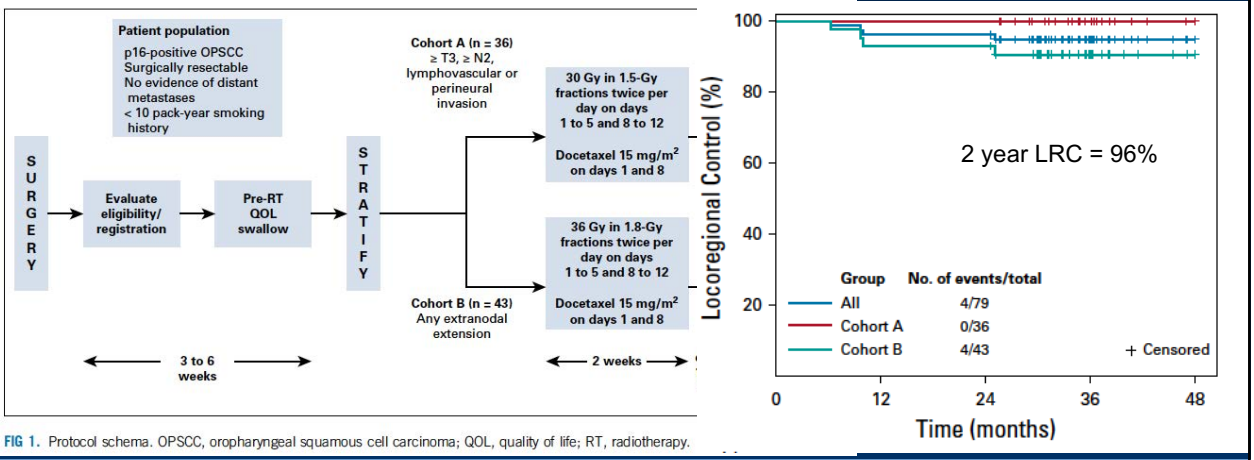

FIG 1. Protocol schema. OPSCC, oropharyngeal squamous cell carcinoma; QOL, quality of life; RT, radiotherapy.

Ma. JCO. 2019.

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Is surgery an option?

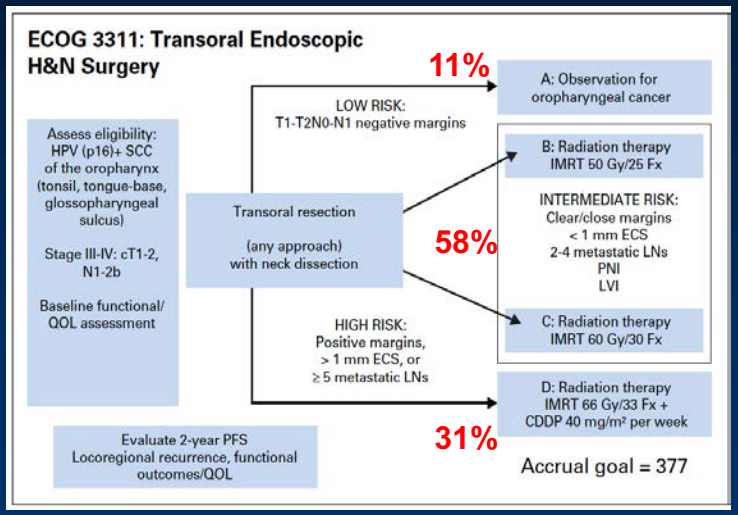
Yes.

TORS = Trans-oral robotic surgery

- Minimally invasive
- Less risks

ECOG 3311:

- Study open since 2013
- Enrolled 511 pts as of 8/1/2018
- Key results this month!?



J Clin Oncol 33:3285-3292.

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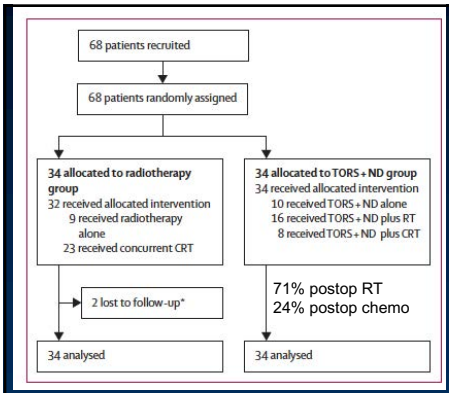

Radiotherapy versus transoral robotic surgery and neck dissection for oropharyngeal squamous cell carcinoma (ORATOR): an open-label, phase 2, randomised trial

Primary endpoint: Dysphagia @ 1 year

	1 year				Clinically meaningful decline*		
	RT group	TORS + ND group	Effect estimate (95% CI)	p value†	RT group	TORS + ND group	p value
Total (primary endpoint)	86·9 (11·4)	80·1 (13·0)	6·7 (0·2 to 13·2)	0·042	7/27 (26%)	11/27 (41%)	0·25
Global	89·6 (15·1)	79·3 (22·6)	10·3 (0·2 to 20·4)	0·046	6/27 (22%)	14/27 (52%)	0·024
Emotional	88·8 (12·0)	81·3 (12·5)	7·4 (0·9 to 14·0)	0·027	5/27 (19%)	13/27 (48%)	0·021
Functional	89·9 (11·5)	86·5 (12·0)	3·4 (−2·9 to 9·6)	0·28	7/27 (26%)	9/26 (35%)	0·49
Physical	83·1 (14·1)	75·3 (16·5)	7·9 (−0·3 to 16·0)	0·058	12/27 (44%)	16/27 (59%)	0·28
Composite (total score excluding global score)	86·7 (11·4)	80·2 (13·1)	6·5 (0·0 to 13·1)	0·049	6/27 (22%)	11/27 (41%)	0·14

Data are presented as mean (SD) unless otherwise stated. RT=radiotherapy. TORS + ND=transoral robotic surgery and neck dissection. *Defined as a decrease of at least 10 points. †p values adjusted for stratification by p16 status (post-hoc analysis): total (p=0·054), global (p=0·071), emotional (p=0·040), functional (p=0·29), physical (p=0·064), and composite (p=0·062).

Table 2: **Quality-of-life scores at 1 year for the MD Anderson Dysphagia Inventory**

Lancet Oncol 2019

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Key Takeaway:

Surgery (TORS) and radiation therapy are both good options for LA-OPSCC.

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How do we treat HPV associated HNSCC at UNC?

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Can we dose reduce both chemo and RT?

Version 1: De-intensified Chemoradiotherapy

1. **60 Gy RT for 6 weeks (*instead of 70 Gy for 7 weeks*)**
2. **Cisplatin 30mg/m^2 for 6 weeks (*instead* of 40mg/m^2 for 7 weeks)**

N=44
Median f/u = 34 months (88% ≥ 2 years)

Primary endpoint (IJROBP 2015):
pCR rate = 86%

Secondary endpoints (Cancer 2018):
3 year PFS = 100%
3 year OS = 95%
Global QoL returned to baseline
Swallowing returned to baseline
Dry mouth continues to improve > 1 year

Phase 2 Trial of De-intensified Chemoradiation Therapy for Favorable-Risk Human Papillomavirus–Associated Oropharyngeal Squamous Cell Carcinoma

Int J Radiation Oncol Biol Phys, Vol. 93, No. 5, pp. 976–985, 2015

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Version 2: Patient Characteristics

	N=114	%
Age (mean)	62 (37-87)	
Male	96	84%
Caucasian	104	91%
Married	90	79%
Tobacco		
Never	54	47%
</= 10 pack years	38	33%
>10 pack years	22	19%
T1-T2 Stage	96	84%
N0-1 Stage	96	84%
HPV/p16 status		
HPV+/p16+	46	40%
HPV-/p16+	12	11%
HPV unk/p16+	56	49%

- 100% received 60 Gy
- Chemotherapy:
  - 89/114 (78%) received chemo
  - 57/89 (64%) received 6 doses cisplatin
  - 10/89 (11%) received cetuximab
- 11 patients had neck dissection (4 pathologically positive)

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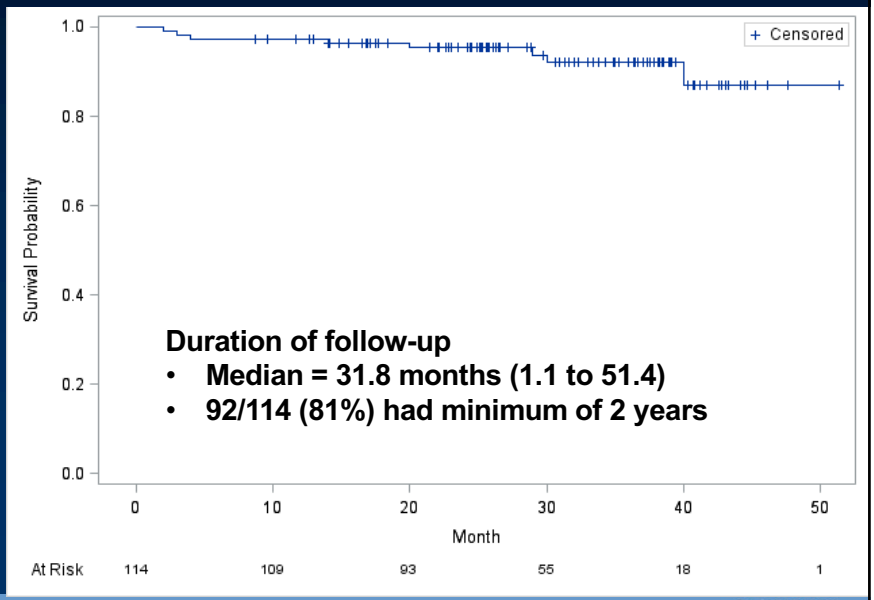
2 Year Outcomes

Local Control	96%
Regional Control	99%
Distant Metastasis Free Survival	91%
Progression Free Survival	**86%**
Overall Survival	95%

Overall Survival



Duration of follow-up
- Median = 31.8 months (1.1 to 51.4)
- 92/114 (81%) had minimum of 2 years

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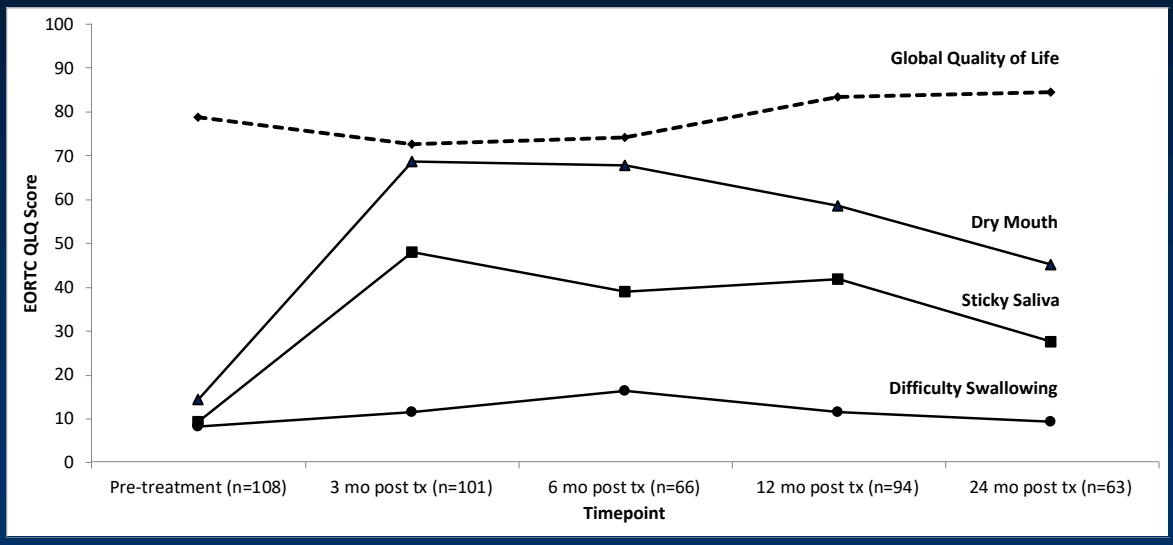
Quality of Life Scores



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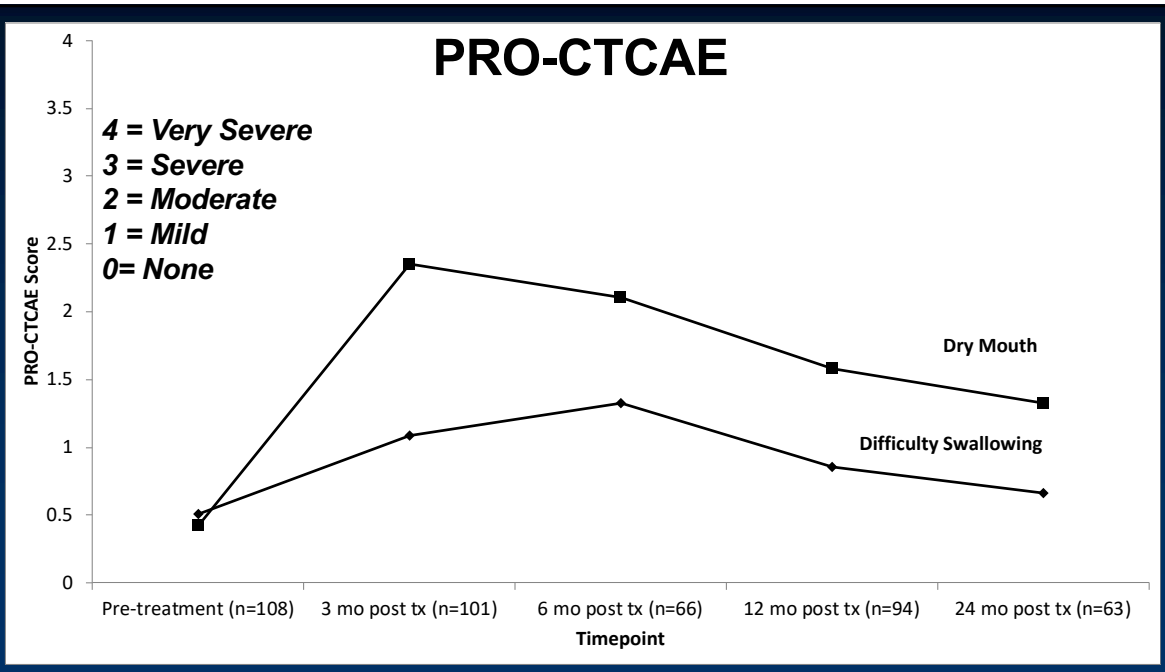
PRO-CTCAE



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Phase II Trial of De-Intensified Chemoradiotherapy for Human Papillomavirus–Associated Oropharyngeal Squamous Cell Carcinoma

Bhishamjit S. Chera, MD[1,2]; Robert J. Amdur, MD[3]; Rebecca Green, MSW[1]; Colette Shen, MD, PhD[1,2]; Gaorav Gupta, MD, PhD[1,2]; Xianming Tan, PhD[2]; Mary Knowles, ANP[1]; David Fried, PhD[1]; Neil Hayes, MPH, MD[4]; Jared Weiss, MD[1,2]; Juneko Grilley-Olson, MD[1,2]; Shetal Patel, MD, PhD[1,2]; Adam Zanation, MD[1]; Trevor Hackman, MD[1]; Jose Zevallos, MPH, MD[5]; Jeffrey Blumberg, MD[1]; Samip Patel, MD[1]; Mohit Kasibhatla, MD[6]; Nathan Sheets, MD[7]; Mark Weissler, MD[1]; Wendell Yarbrough, MMHC, MD[1,2]; and William Mendenhall, MD[3]

Journal of Clinical Oncology®

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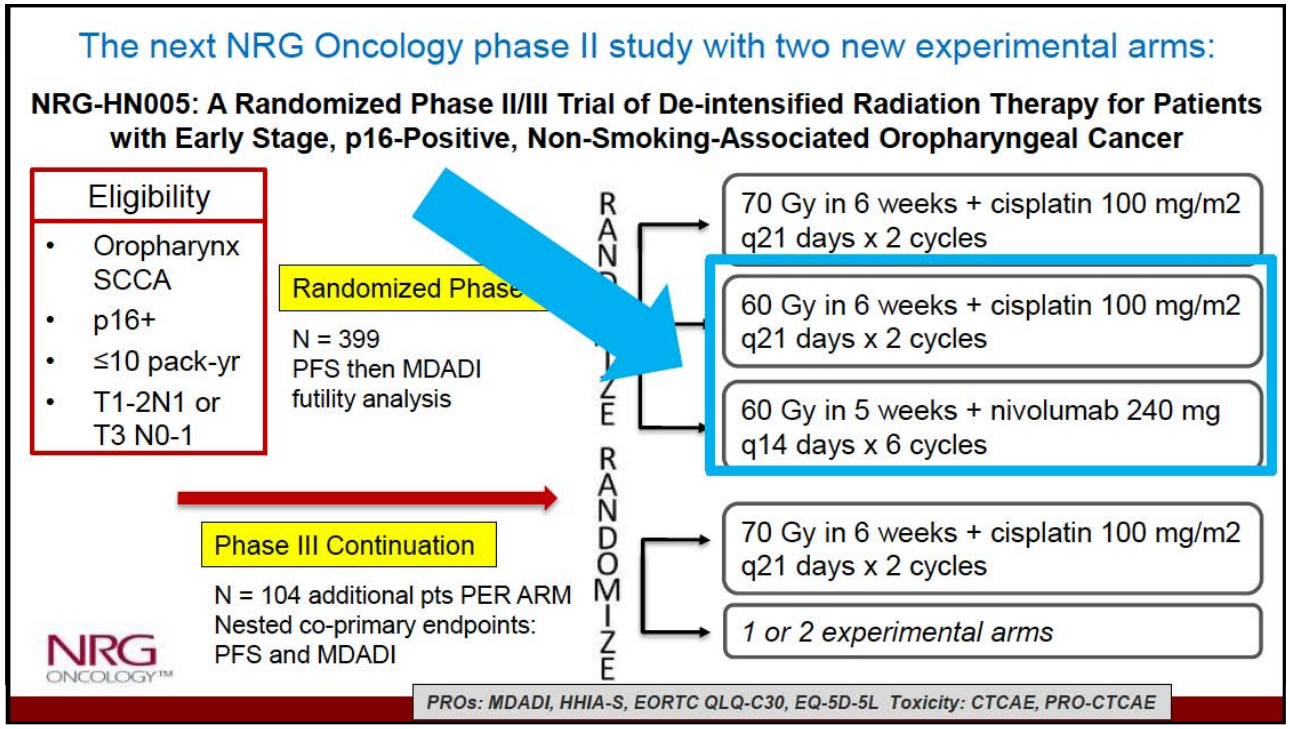
Lots of data.

How will the field move forward?

50



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Biomarker strategies in HNSCC

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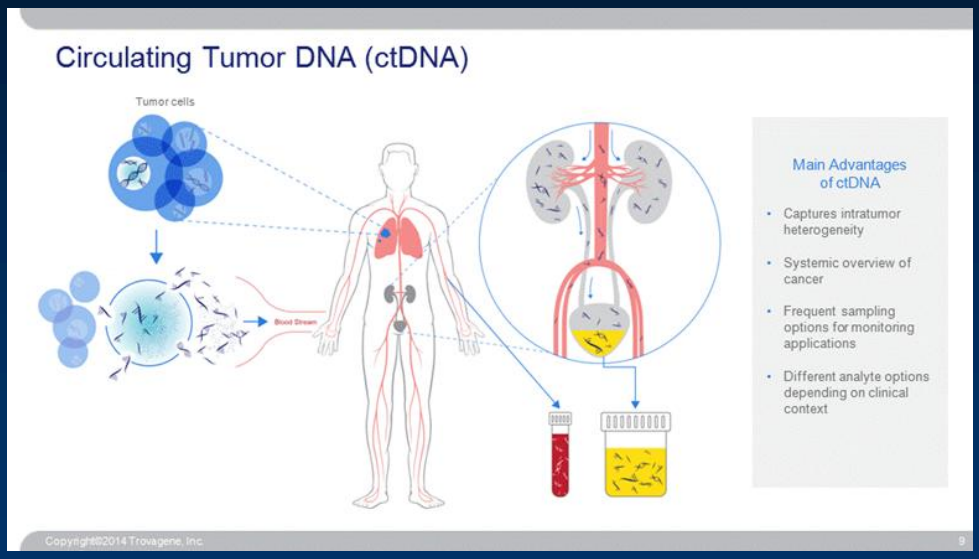
Liquid Biomarkers



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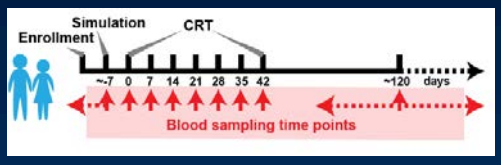
ctDNA as a circulating biomarker of treatment response for HPV-related HNSCC

Since 2016, our UNC group has prospectively analyzed ctHPVDNA

- 3 clinical trials (LCCC 1121,1413,1612)
- ~160 patients, >1500 blood samples to date



Ultimate goal of ctDNA:

1. Guide therapeutic intensity
2. Earlier detection of disease recurrence

Chera. JCO. 2020

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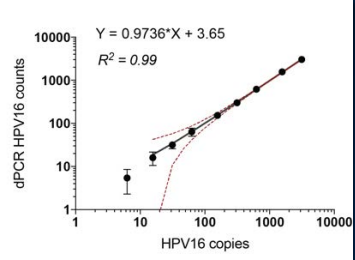
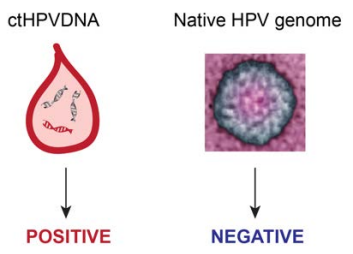
Multi-analyte digital PCR (dPCR) assay for ctHPVDNA





- Standardized multi-step analytical protocol to optimize specificity and sensitivity
- Distinguishes fragmented ctDNA from native viral genomes
- Detects ctHPV16, 18 ,31, 33, and 35 *(more high-risk strains coming)*
- **Linear:** absolute quantification over 5 orders of magnitude (5-50,000 copies)
- **Precise:** High reproducibility
- **Sensitive:** Detects as few as 6 copies of HPV16 with ~80% sensitivity

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Is ctHPVDNA detectable?

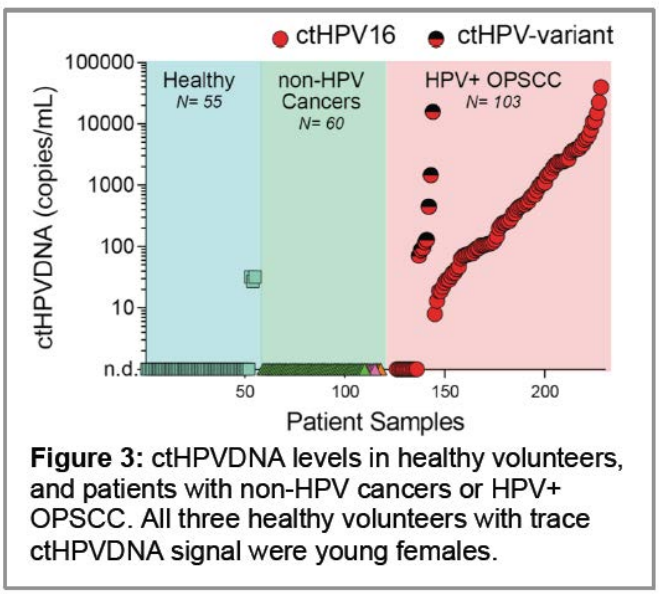

Figure 3: ctHPVDNA levels in healthy volunteers, and patients with non-HPV cancers or HPV+ OPSCC. All three healthy volunteers with trace ctHPVDNA signal were young females.

Cohort of 218 pts
- 55 healthy (no cancer)
- 60 non-HPV cancer patients
- 103 non-metastatic HPV-OPSCC patients (p16 IHC+)

98% Specificity
89% Sensitivity

Hypothesize:
- 11 ctHPVDNA-negative pts were false positives of the p16 IHC assay
- May be HPV negative OPSCC

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Precision Medicine and Imaging

Clinical Cancer Research

Rapid Clearance Profile of Plasma Circulating Tumor HPV Type 16 DNA during Chemoradiotherapy Correlates with Disease Control in HPV-Associated Oropharyngeal Cancer

Bhishamjit S. Chera[1,2], Sunil Kumar[1,2], Brian T. Beaty[1], David Marron[2,3], Stuart Jefferys[2,3], Rebecca Green[1], Emily C. Goldman[1], Robert Amdur[4], Nathan Sheets[5], Roi Dagan[6], D. Neil Hayes[7], Jared Weiss[2,8], Juneko E. Grilley-Olson[2,8], Adam Zanation[9], Trevor Hackman[9], Jeffrey M. Blumberg[9], Samip Patel[9], Mark Weissler[9], Xianming M. Tan[2,10], Joel S. Parker[2,3,11], William Mendenhall[4], and Gaorav P. Gupta[1,2]

- Multi-institutional prospective biomarker trial
- N=103
- p16+ OPSCC
- Definitive CRT
- Blood specimens baseline, weekly during CRT

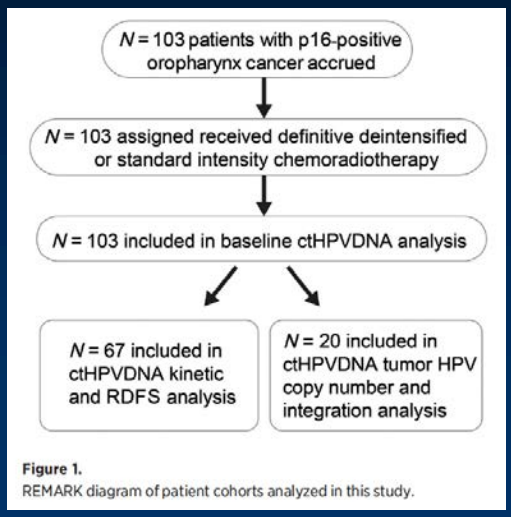

Figure 1.
REMARK diagram of patient cohorts analyzed in this study.

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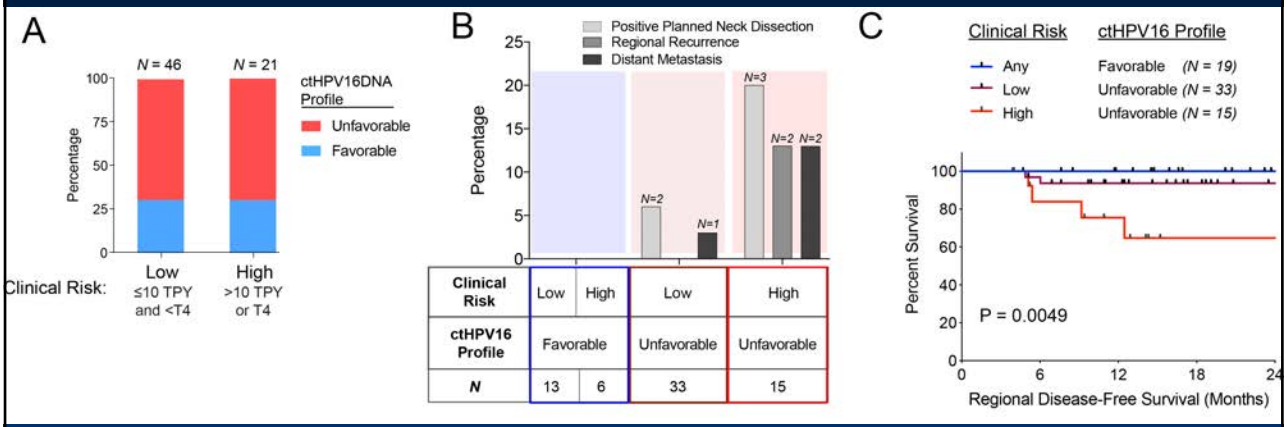
Favorable ctHPV16DNA clearance profile correlates with disease control



Favorable ctHPV16DNA clearance profile = high baseline copy number (>200 copies/mL) and >95% clearance of ctHPV16DNA by day 28 of CRT.

Chera B, …, Gupta G *Clinical Cancer Research* (2019)

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PLASMA CIRCULATING TUMOR HPV DNA FOR THE SURVEILLANCE OF CANCER RECURRENCE IN HPV-ASSOCIATED OROPHARYNGEAL CANCER

Chera BS, Kumar S, Shen C, Amdur RJ, Dagan R, Green R, Goldman E, Weiss J, Grilley-Olson J, Patel S, Zanation A, Hackman T, Blumberg J, Patel S, Thorp B, Weissler M, Yarbrough W, Sheets N, Mendenhall W, Tan XM, Gupta GP.

Journal of Clinical Oncology. 2020

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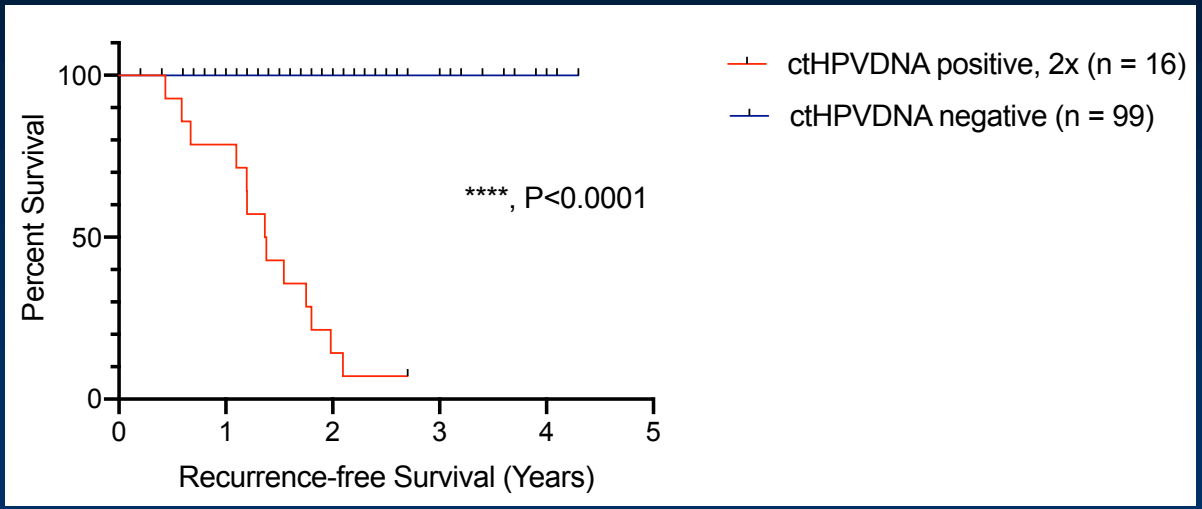
ctHPVDNA relapse predicts clinical recurrence



Chera. Journal of Clinical Oncology. 2020

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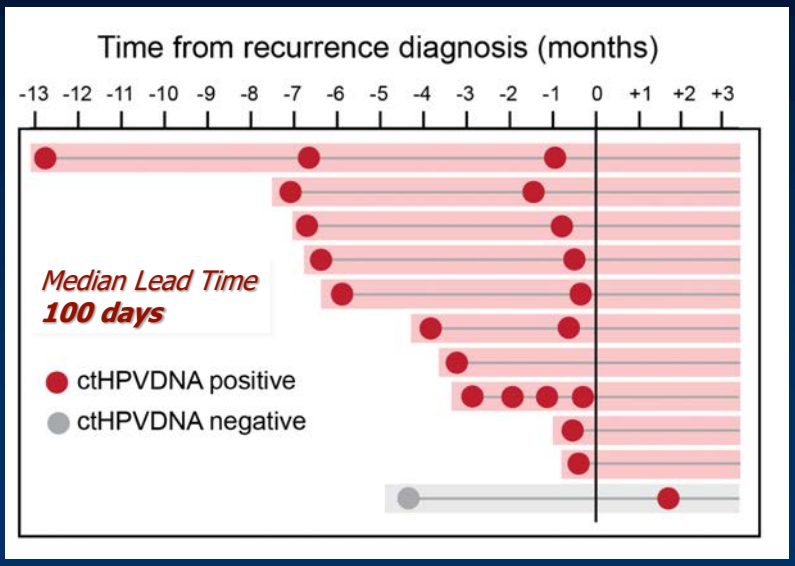
Early detection of recurrence by ctHPVDNA



Chera. Journal of Clinical Oncology. 2020

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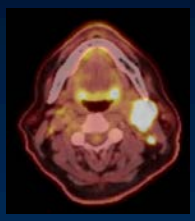
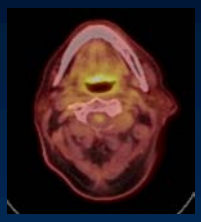
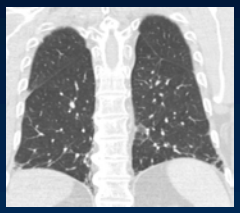
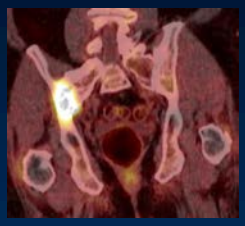
Case Example

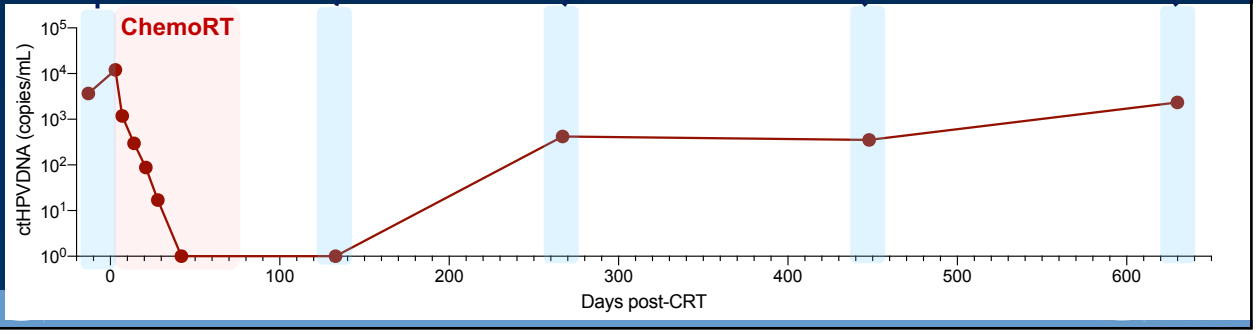





T1N1 L BOT SCC (p16+)

PET ➔ CR

Neck/Chest CT ➔ NED

PET ➔ biopsy
bone metastasis



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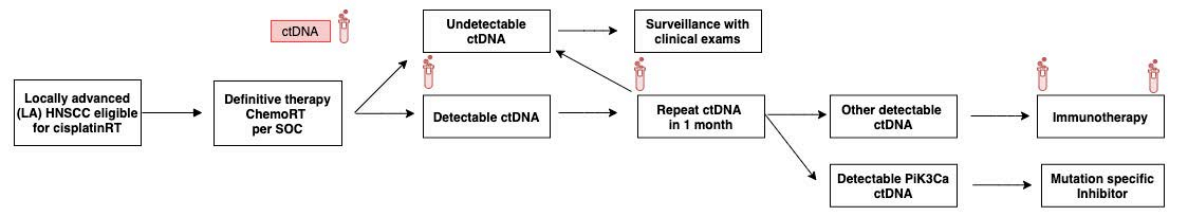
Clinical trial to evaluate early detection of recurrence

Pan-HPV approach



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Key Takeaways for ctHPVDNA

- Plasma ctHPVDNA surveillance testing has high NPV and PPV for early detection of cancer recurrence
- ctHPVDNA based surveillance may reduce the overall cost of post-treatment surveillance in patients who remain ctDNA negative
  - Less radiographic scans
- Prospective evaluation in a clinical trial is needed. Efforts are underway

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What about ctDNA in HPV negative patients?

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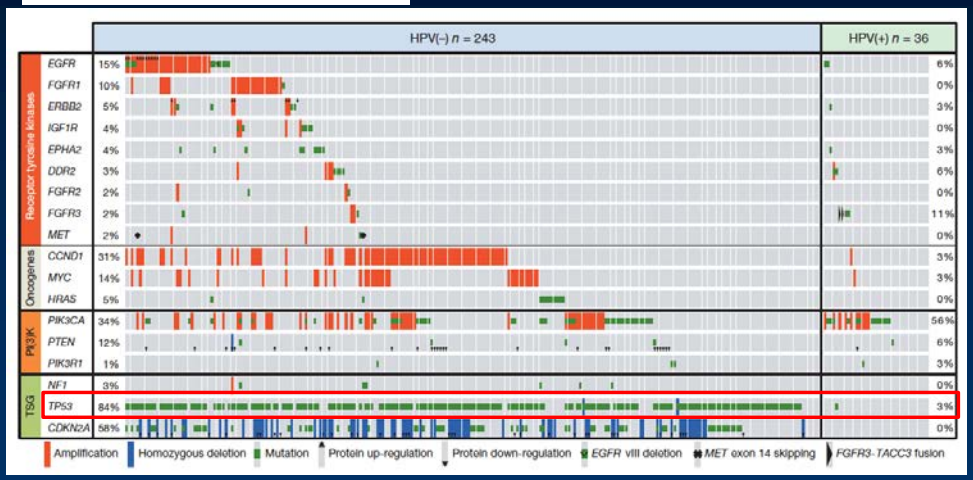
Comprehensive genomic characterization of head and neck squamous cell carcinomas

NATURE | VOL 517 | 29 JANUARY 2015



P53 is the *"guardian of the genome"*

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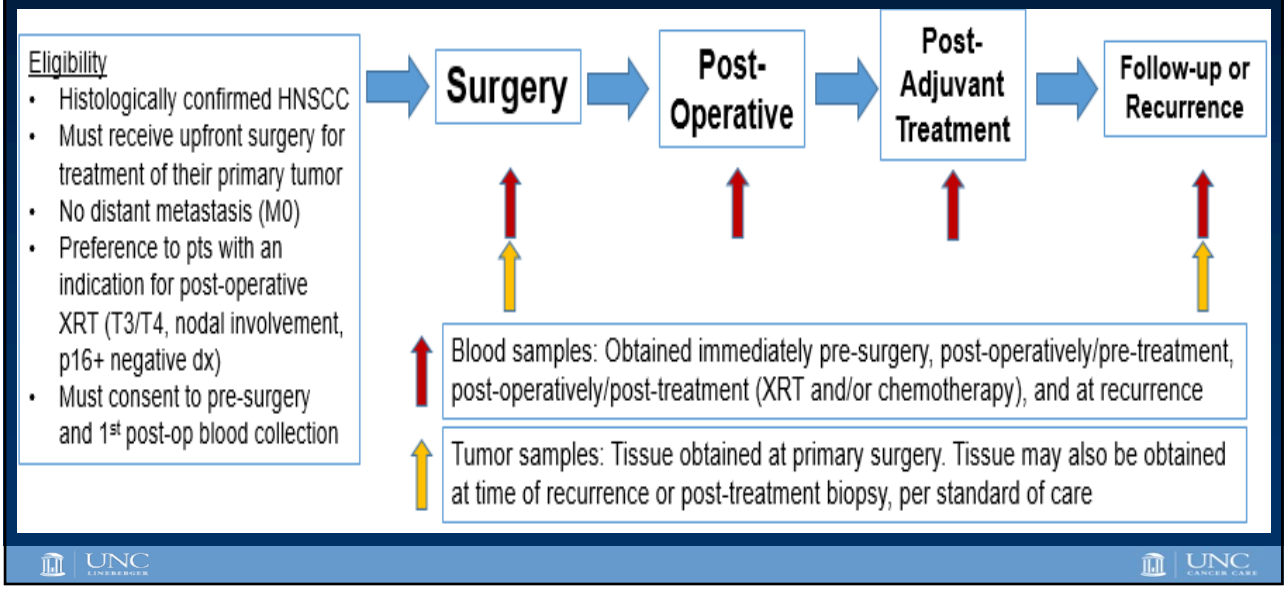
LCCC 1835 Study Schema



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LCCC 1835 Study Aims

Aim 1: To estimate the feasibility of detecting ctDNA in pre-operative plasma
- Targeted NGS sequencing on surgically excised tumor tissue
- Design and validate tumor-specific mutation (TSM) assays for detection by digital droplet PCR

Aim 2: To estimate the feasibility of detecting ctDNA in post-operative plasma and explore associations with outcomes
- Quantify changes in plasma ctDNA following surgical resection
- Investigate the correlation of pathological risk factors and disease-free survival

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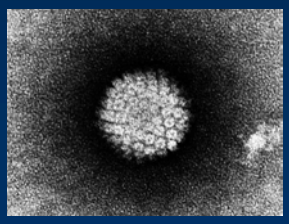
Past

2020



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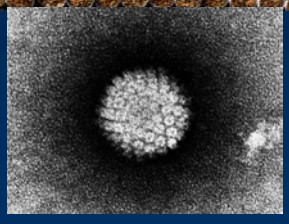
2030??



Basic Science ⟷ Translational Research ⟷ Clinical Trials

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Case Revisited

Ramses Heel is a 55 year old presents who presented with a painless neck mass. PMH of hypertension and asthma. Family history of breast cancer (mother and older sister). Admits to a 5 pack year smoking history during college and social alcohol use currently. He travels to China yearly for business for the last 10 years. Your order an neck ultrasound and CT scan which shows a 3cm neck mass. FNA positive for squamous cell carcinoma.

Your patient asks what caused his cancer?

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Question #2

55 y/o WM p/w painless neck mass. PMH HTN and asthma, FamHx breast ca. SocHx +5 PYH, ~EtOH, +China travel. CT with 5cm neck mass. FNA +SCC

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Question #2

What is the most likely risk factor for his head and neck cancer?

1. Smoking history
2. Social alcohol use
3. Age
4. Yearly travel to China
5. Human papilloma virus (HPV)

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Question #3

Following a negative CT chest, Ramses final diagnosis is a locally advanced HPV-associated right tonsillar SCC. Stage is T1N1M0

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Question #3

Which HPV subtype is most likely associated with Ramses' cancer?

1. HPV 11
2. HPV 16
3. HPV 18
4. HPV 31
5. HPV 33

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Question #4

Ramses meet with ENT, radonc, medonc. He is confused about the different tx options and seeks your advice?

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Question #4

Based on the following options, what is the best treatment for his T1N1 HPV+ OPSCC?

1. Observation with repeat CT scans in 3 months
2. Vaccination with Gardasil
3. Surgery followed by adjuvant chemotherapy
4. Concurrent chemoradiation therapy
5. Hospice

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Conclusions

1. Head and neck cancers are common
   - Location of cancer may suggest associated risk factor
   - The incidence of oropharynx due to HPV is rising
2. HPV associated cancers are lower risk compared to smoking related HNSCC
   - Treatment deintensification will be come standard of care (when *not* if)
   - How to "best" de-intensify is still an active area of investigation
3. Biomarkers are important for cancer diagnosis, treatment, and surveillance
   - Testing for ctHPVDNA may soon become part of standard practice. How to use this assay to guide treatment decisions is being studied
   - ctDNA based on gene mutational status is also being studied for non-HPV associated HNSCC

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Acknowledgements

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Our Patients

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Thank you!

Questions?

Contact: Siddharth_sheth@med.unc.edu

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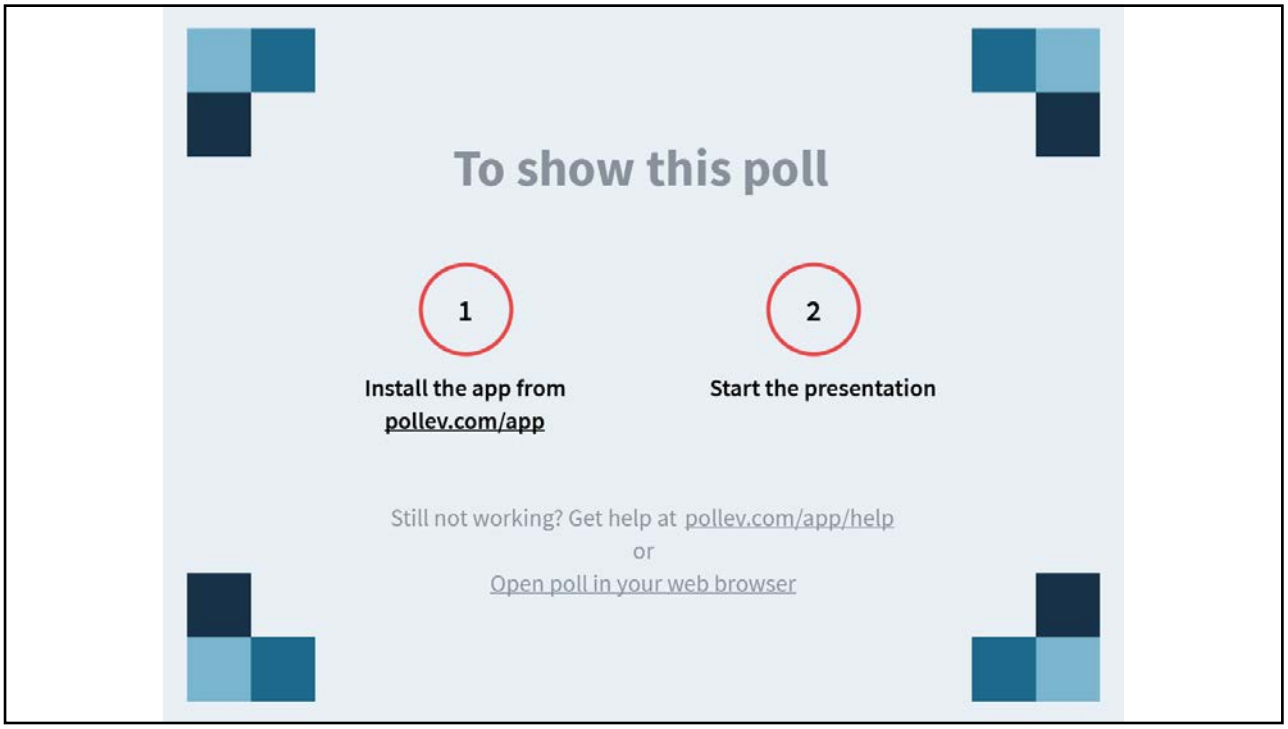

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THANK YOU!

University Cancer Research Fund

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UNC Cancer Network Telehealth Team

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Mary King, *Operational Coordinator*
Veneranda Obure, *A/V Support Engineer*
Jon Powell, PhD, *Continuing Education Specialist*

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THANK YOU FOR PARTICIPATING!

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UPCOMING LIVE LECTURES

CANCER TREATMENT IN NORTH CAROLINA **PATIENT CENTERED CARE**

Live Lecture

May 13

12:00 PM

Delivering Survivorship Care in North Carolina

Deborah Mayer, PhD, RN, AOCN, FAAN

CANCER TREATMENT IN NORTH CAROLINA **RESEARCH TO PRACTICE**

Live Lecture

May 27

12:00 PM

Gastrointestinal Cancer Management in North Carolina: Updates for 2020

Michael S. Lee, MD

For a complete listing and details on coming events visit:

www.unccn.org/events

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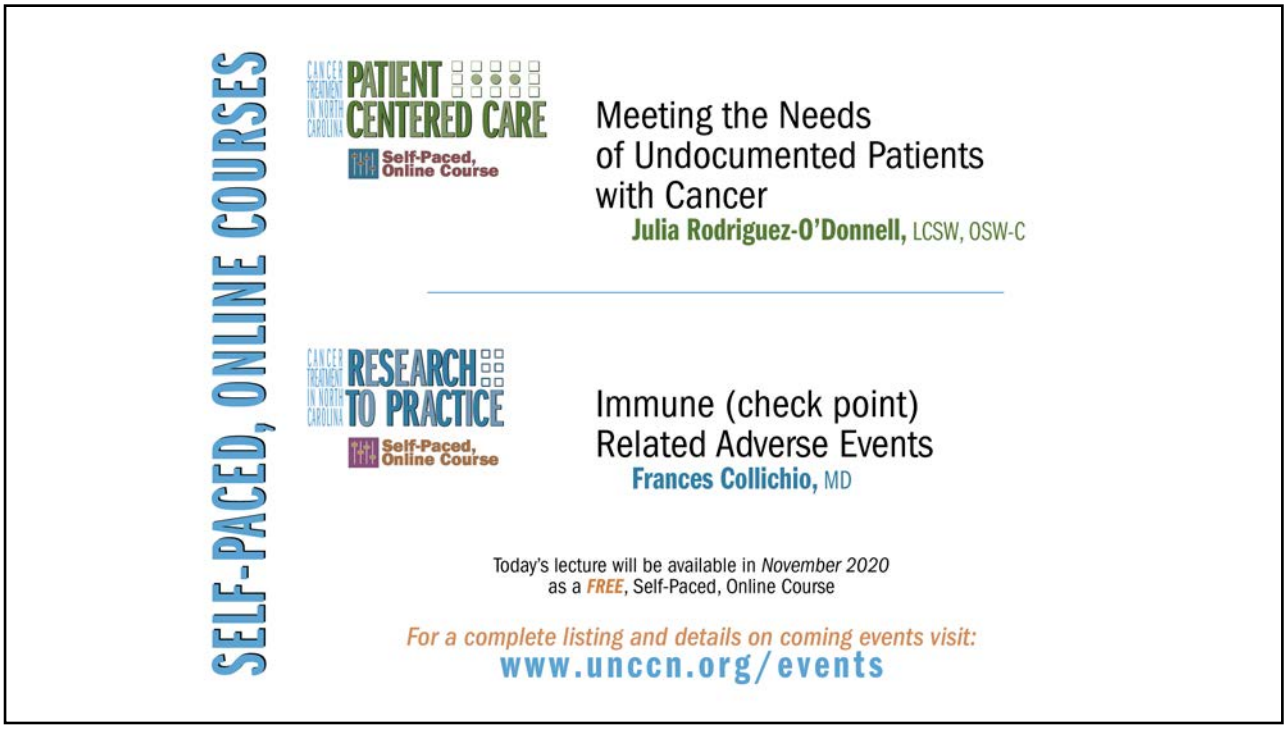
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Self-Paced, Online Course
Immune (check point) Related Adverse Events
Frances Collichio, MD
Today's lecture will be available in November 2020 as a FREE, Self-Paced, Online Course
For a complete listing and details on coming events visit:
www.unccn.org/events

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